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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2008-D-0128 (formerly Docket No. 2007D-0396)]

How Should Liver Injury and Dysfunction Caused by Drugs Be Measured, Evaluated, and Acted Upon in Clinical Trials?

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public conference.

SUMMARY: The Food and Drug Administration (FDA) is announcing a public conference entitled "How Should Liver Injury and Dysfunction Caused by Drugs Be Measured, Evaluated, and Acted Upon in Clinical Trials?" This conference will be cosponsored with the Critical Path Institute (C-Path). The purpose of the conference is to discuss, debate, and share views among stakeholders in academia, patient groups, regulatory bodies, and the health care and pharmaceutical industries on how best to measure, evaluate, and act upon liver injury and dysfunction caused by drugs used during clinical trials.

DATES: This public conference will be held on March 23, 2016, from 8 a.m. to 6 p.m., and on March 24, 2016, from 8 a.m. to 4 p.m.

ADDRESSES: This public conference will be held at the College Park Marriott Hotel & Conference Center, 3501 University Blvd., East Hyattsville, MD 20783. The hotel's phone number is 301-985-7300.

FOR FURTHER INFORMATION CONTACT: Lana L. Pauls, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 4478, Silver Spring, MD 20993-0002, 301-796-0518, lana.pauls@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

In July 2009, FDA announced the availability of a guidance for industry entitled "Drug-Induced Liver Injury: Premarketing Clinical Evaluation" (74 FR 38035, July 30, 2009, https://www.gpo.gov/fdsys/pkg/FR-2009-07-30/pdf/E9-18135.pdf). First, this guidance explains that drug-induced liver injury (DILI) has been the most frequent cause of safety-related drug marketing withdrawals over the past 50 years and that hepatotoxicity has both limited the use of many drugs that have been approved and prevented the approval of others. Second, this guidance discusses methods of detecting DILI by periodic tests of serum enzyme activities and of bilirubin concentration and how changes in the results of these laboratory tests over time, along with symptoms and physical findings, may be used to estimate the severity of the injury. Third, this guidance suggests some "stopping rules" for interrupting drug treatment and mentions the need to obtain sufficient clinical information to assess causation. FDA published a draft of this guidance in 2006, and comments on that draft were taken into consideration when issuing the final guidance in July 2009.

II. Conference Information

The purpose of the 2016 conference is to invite participants to present their data and views and to hold an open discussion. The meetings in recent years have been attended by members of industry, regulatory bodies, and academic consultants, and the topics discussed have included several unresolved issues on which consensus was sought.

Registration: A registration fee ($650 for industry registrants and $325 for Federal government and academic registrants) will be charged to help defray the cost of renting the meeting space, providing meals and snacks, and covering the travel fees incurred by invited

academic (but not government or industry) speakers, as well as any other expenses. The registration process will be handled by C-Path, an independent, nonprofit organization established in 2005 with public and private philanthropic support from the southern Arizona community, Science Foundation Arizona, and FDA.

Additional information on the conference, program, and registration procedures may be obtained on the Internet at http://www.c-path.org, and at http://www.fda.gov by typing "liver toxicity" into the search box. (FDA has verified the Web site addresses but is not responsible for any subsequent changes to the Web sites after this document publishes in the Federal Register.)

Transcripts: Please be advised that as soon as a transcript is available, it will be accessible at http://www.regulations.gov. It may be viewed at the Division of Dockets Management, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD. A transcript will also be available in either hardcopy or on CD-ROM, after submission of a Freedom of Information request. The Freedom of Information office address is available on the Agency's Web site at http://www.fda.gov.

Materials presented at past programs (from 2007 to 2015) (including copies of slides shown, comments made about the slides, and discussions following the slides) may be accessed at http://www.aasld.org/events-professional-development/drug-induced-liver-injury-2015-program. (FDA has verified this Web site address but is not responsible for any subsequent changes to it after this document publishes in the Federal Register.)

Dated: January 8, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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